DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Memorandum

Date SEP 25 1996

From Director, Office of Device Evaluation (HFZ-400)
Center for Devices and Radiological Health (CDRH)

Subject Premarket Approval of Allergan Optical's Refresh® CL Lubricating and Rewetting Drops - ACTION

To The Director, CDRH
ORA _____

ISSUE. Publication of a notice announcing approval of the subject PMA.

FACTS. Tab A contains a FEDERAL REGISTER notice announcing:

(1) a premarket approval order for the above referenced medical device (Tab B); and

(2) the availability of a summary of safety and effectiveness data for the device (Tab C).

RECOMMENDATION. I recommend that the notice be signed and published.

Susan Alpert, Ph.D., M.D.

Attachments
Tab A - Notice
Tab B - Order
Tab C - S & E Summary

DECISION

Approved ___ Disapproved ___ Date _____

Prepared by Eleanor M. Felton, CDRH, HFZ-460, August 7, 1996, 594-1744

DEPARTMENT OF HEALTH AND HUMAN SERVICES

DRAFT

FOOD AND DRUG ADMINISTRATION

[DOCKET NO. _____]

ALLERGAN OPTICAL; PREMARKET APPROVAL OF Refresh® CL Lubricating and Rewetting Drops

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing its approval of the application by Allergan Optical, Irvine, CA, for premarket approval, under section 515 of the Federal Food, Drug, and Cosmetic Act (the act), of Refresh® CL Lubricating and Rewetting Drops. FDA's Center for Devices and Radiological Health (CDRH) notified the applicant, by letter on September 25, 1996, of the approval of the application.

DATES: Petitions for administrative review by (insert date 30 days after date of publication in the FEDERAL REGISTER).

ADDRESSES: Written requests for copies of the summary of safety and effectiveness data and petitions for administrative review, to the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1-23, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT:

James F. Saviola, O.D.,

Center for Devices and Radiological Health (HFZ-460),

Food and Drug Administration,

9200 Corporate Blvd.,

Rockville, MD 20850,

301-594-1744.

SUPPLEMENTARY INFORMATION: On May 6, 1996, Allergan Optical, Irvine, CA 92713-9534, submitted to CDRH an application for premarket approval of Refresh® CL Lubricating and Rewetting Drops. The device is a lubricating and rewetting solution and is indicated for the lubrication and rewetting of soft contact lenses and helps to relieve dryness, discomfort and irritation that may be associated with lens wear.

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Ophthalmic Devices Panel of the Medical Devices Advisory Committee, an FDA advisory panel, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

On September 25, 1996, CDRH approved the application by a letter to the applicant from the Director of the Office of Device Evaluation, CDRH.

A summary of the safety and effectiveness data on which CDRH based its approval is on file in the Dockets Management Branch (address above) and is available from that office upon written request. Requests should be identified with the name of the device and the docket number found in brackets in the heading of this document.

Opportunity For Administrative Review

Section 515(d)(3) of the act (21 U.S.C. 360e(d)(3)) authorizes any interested person to petition, under section 515(g) of the act, for administrative review of CDRH's decision to approve this application. A petitioner may request either a formal hearing under part 12 (21 CFR part 12) of FDA's administrative practices and procedures regulations or a review of the application and CDRH's action by an independent advisory committee of experts. A petition is to be in the form of a petition for reconsideration under 10.33(b) (21 CFR 10.33(b)). A petitioner shall identify the form of review requested (hearing or independent advisory committee) and shall submit with the petition supporting

data and information showing that there is a genuine and substantial issue of material fact for resolution through administrative review. After reviewing the petition, FDA will decide whether to grant or deny the petition and will publish a notice of its decision in the FEDERAL REGISTER. If FDA grants the petition, the notice will state the issue to be reviewed, the form of the review to be used, the persons who may participate in the review, the time and place where the review will occur, and other details.

Petitioners may, at any time on or before (insert date 30 days after date of publication in the FEDERAL REGISTER), file with the Dockets Management Branch (address above) two copies of each petition and supporting data and information, identified with the name of the device and the docket number found in brackets in the heading of this document. Received petitions may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

This notice is issued under the Federal Food, Drug, and Cosmetic Act (secs. 515(d)(3), 520(h) (21 U.S.C. 360e(d), 360j(h))) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.10) and redelegated to the Director, Center for Devices and Radiological Health (21 CFR 5.53).

Dated:_____.

_____

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Mr. Paul J. Nowacki
Manager, Regulatory Affairs
Allergan Optical
2525 Dupont Drive
P.O. Box 19534
Irvine, CA 92713-9534

SEP 25 1996

Re: P960012
Refresh® CL Lubricating and Rewetting Drops
Filed: May 6, 1996
Amended: August 21, and September 12 and 17, 1996

Dear Nowacki:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for Refresh® CL Lubricating and Rewetting Drops. This device is indicated for the lubrication and rewetting of soft contact lenses and helps to relieve dryness, discomfort and irritation that may be associated with lens wear. We are pleased to inform you that the PMA is approved subject to the conditions described below and in the "Conditions of Approval" (enclosed). You may begin commercial distribution of the device upon receipt of this letter.

Expiration dating for this device has been established and approved at 30 months for the 0.01 fl. oz. single dose containers. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(8).

CDRH will publish a notice of its decision to approve your PMA in the FEDERAL REGISTER. The notice will state that a summary of the safety and effectiveness data upon which the approval is based is available to the public upon request. Within 30 days of publication of the notice of approval in the FEDERAL REGISTER, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the Federal Food, Drug, and Cosmetic Act (the act).

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form.

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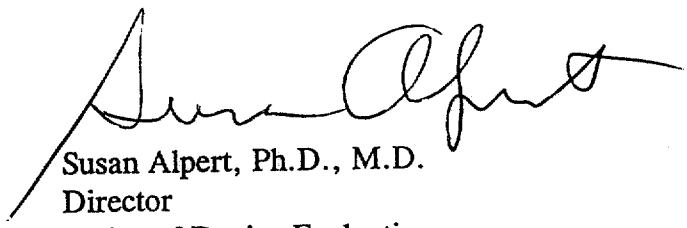
All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

If you have any questions concerning this approval order, please contact Mrs. Eleanor M. Felton or James F. Saviola, O.D. at (301) 594-1744.

Sincerely yours,



Susan Alpert, Ph.D., M.D.
Director
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

Summary of Safety and Effectiveness

I. General Information

A. Premarket Approval Application (PMA) Number: P960012
Date Filed: May 6, 1996
Date Approved:
SEP 25 1996

B. Device Generic Name: lubricating and rewetting solution

C. Device Trade Name: Refresh® CL Lubricating and Rewetting Drops

D. Applicant's Name and Address: Allergan Optical
2525 Dupont Drive
P.O. Box 19534
Irvine, CA 92713-9534

E. Good Manufacturing Practice (GMP) Inspection:
Dates of Inspection: April 7, 1995; and January 29, 1996
Conclusion: The manufacturing site was found to be in compliance with device GMP requirements.

II. Indications

Refresh® CL Lubricating and Rewetting Drops are indicated for the lubrication and rewetting of soft contact lenses and help to relieve dryness, discomfort and irritation that may be associated with lens wear.

III. Summary

The applicant performed non-clinical and clinical testing on the device in accordance with the FDA Testing Guidelines for Class III Soft (Hydrophilic) Contact Lens Solutions dated July 1985. The non-clinical testing supports the safety and effectiveness of the device from microbiology, toxicology, chemistry and manufacturing perspectives. Data were evaluated from a controlled, randomized, double-masked, multicenter parallel group clinical study consisting of 444 eyes in the Test Group using the subject device and 194 eyes in a Control Group using the Lens Plus® Rewetting Drops. The subjects in both groups were followed for 6 months and clinically evaluated. The Test Group included 54 males and 168 females and the Control Group included 20 males and 77 females which is representative of the contact lens wearing population in the United States. Based on the detailed analysis of the data presented in the PMA, it was determined that the clinical findings for the Control Group and Test Group, i.e., adverse reactions, positive slit lamp findings, patient symptoms, problems and complaints, visual acuity, lens replacements, discontinued patients, and lens wearing time were within expected limits for soft contact lens wearers. Any differences in these groups do not raise concerns about the safety and

effectiveness of the device when accompanied by appropriate labeling. Although the potential exists for minor differences in physiological response by gender for the target population, the minimal number of clinically significant findings does not indicate gender difference to be of clinical importance for this device.

IV. Safety and Effectiveness Data

A. Non-clinical Data

The applicant conducted a battery of in-vivo and in-vitro acute toxicology studies that support the safety and biocompatibility of the solution with soft (hydrophilic) contact lens materials. Additionally, chemistry and manufacturing information was submitted demonstrating that the solution is suitable for use to lubricate and rewet soft (hydrophilic) lens materials. The adequacy of the manufacturing process, including sterilization and shelf-life expiration dating, was established through a review of the manufacturing and microbiology data submitted in the PMA as well as through an on-site GMP inspection.

B. Clinical Data (Test Group)

Accountability (496 eyes enrolled): 444 completed and 52 discontinued (none associated with pathology)

Visual Acuity:	Initial Visit with Lens	Final Visit with Lens
20/30 or better	441	443
20/40 or worse	3	1

Wear Time:	Initial Adapted (1 week)	Final (6 months)
Daily	13.8 hours	14 hours

Adverse Reactions: None for all eyes enrolled

Slit Lamp Findings:	Initial Visit (94/444 eyes)=21.2%	Final Visit (95/444 eyes)=21.4%
Staining	29	30
Vascularization	10	8
Injection	21	20
Tarsal Abnormalities	25	28
Other	9	9

Symptoms, Problems, Complaints:	(410 reports/3724 exams)=11.0%
Categories reported=10	
Vision Related (e.g. variable vision)	(89/410)=21.7%
Comfort (e.g. dryness, pain, itching)	(291/410)=71.0%
All Other	(30/410)=7.3%

Lens Replacements:	(161 replaced/444 dispensed)=36.3%
Categories reported=9	
Vision Related (e.g. refractive change)	(30/161)=18.6%
Lens Related (e.g. damaged)	(65/161)=40.4%
Other (e.g. rechallenge, lost)	(66/161)=41.0%

C. Clinical Data (Control Group)

Accountability (210 eyes enrolled): 194 completed and 16 discontinued (none associated with pathology)

Visual Acuity:	Initial Visit with Lens	Final Visit with Lens
20/30 or better	194	194
20/40 or worse	0	0

Wear Time:	Initial Adapted (1 week)	Final (6 months)
Daily	13.8 hours	14.0 hours

Adverse Reactions: None reported for all eyes enrolled

Slit Lamp Findings:	Initial Visit (34/194 eyes)=17.5%	Final Visit (32/194 eyes)=16.5%
Staining	11	6
Vascularization	2	4
Injection	4	6
Tarsal Abnormalities	17	16
Other	0	0

Symptoms, Problems, Complaints:	(169 reports/1408 exams)=12.0%
Categories reported=10	
Vision Related (e.g. blurry vision)	(25/169)=14.8%
Comfort (e.g. dryness, itching)	(139/169)=82.2%
All Other	(5/169)=3.0%

Lens Replacements:	(49 replaced/194 dispensed)=25.3%
Categories reported=9	
Vision Related (e.g. refractive change)	(3/49)=6.1%
Lens Related (e.g.damaged)	(17/49)=34.7%
Other (e.g. deposits, lost)	(29/49)=59.2%

The difference in slit lamp findings between the test and control groups, summarized at the initial and final visits, was not clinically significant since all the findings at these visits were graded as grade 1 - trace, except for one grade 2 - mild.

V. Conclusion

The Center for Devices and Radiological Health (CDRH) reviewed the PMA and concluded that the PMA contained sufficient valid scientific evidence to provide reasonable assurance of the safety and effectiveness of the device for the prescribed indications for use. This PMA was not referred to the Ophthalmic Devices Panel, an FDA advisory panel, for review and recommendation because the information in the PMA submission duplicated information previously reviewed by that panel. CDRH approved this PMA in a letter to the applicant dated SEP 25 1998 and signed by the Director, Office of Device Evaluation.

Revised: 9/16/96

Refresh® CL Lubricating and Rewetting Drops (8197X)

Carton

FRONT PANEL

(logo) ALLERGAN

Refresh® CL Lubricating and Rewetting Drops

(carboxymethylcellulose sodium) 0.5%

For soft (hydrophilic) contact lenses.

Preservative free

XX single use containers [0.4 mL](0.01 fl oz each) STERILE

BACK PANEL

Contains: carboxymethylcellulose sodium, calcium chloride, magnesium chloride, potassium chloride, purified water, sodium chloride and sodium lactate. May also contain hydrochloric acid and/or sodium hydroxide to adjust pH.

Directions: To open, COMPLETELY TWIST OFF TAB. Do not pull off. Instill 1 or 2 drops in the affected eye(s) and discard container.

Indications: For lubricating and rewetting of soft contact lenses and to help relieve dryness, discomfort and irritation that may be associated with lens wear.

Contraindications: Do not use if allergic to any ingredient.

UPC Barcode area

Questions or Comments
Please call 1-800-347-5005 8 am - 5 pm Pacific Time

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Refresh® CL Lubricating and Rewetting Drops (8197X)

Carton

RIGHT SIDE PANEL

Warnings: PROBLEMS WITH CONTACT LENSES AND LENS CARE PRODUCTS COULD RESULT IN SERIOUS INJURY TO THE EYE. Follow your eye care practitioner's directions and all labeling instructions for proper use and care of your lenses and lens care products, including the lens case. **EYE PROBLEMS, INCLUDING CORNEAL ULCERS, CAN DEVELOP RAPIDLY AND LEAD TO LOSS OF VISION.** Daily wear lenses: •not indicated for overnight wear, •should not be worn while sleeping. Contact lens wearers should see their eye care practitioner twice each year or if directed, more frequently.

Precautions:

- •To avoid contamination, do not touch tip of container to any surface.
- •Do not reuse. Once opened, discard. Use immediately after opening.
- •Use only if single-use container is intact.
- •Do not touch unit-dose tip to eye.
- •If solution changes color or becomes cloudy, do not use.
- •Keep out of the reach of children.
- •Store at room temperature.
- •Use before the expiration date marked on the container tab and carton.

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Refresh® CL Lubricating and Rewetting Drops (8197X)

Carton

LEFT SIDE PANEL

Adverse Reactions:

The following may occur:

- •Eyes stinging, burning, or itching (irritation)
- •Excessive watering (tearing) of the eyes
- •Unusual eye secretions
- •Redness of the eyes
- •Reduced sharpness of vision (visual acuity)
- •Blurred vision
- •Sensitivity to light (photophobia)
- •Dry eyes

If any of the above occur, a serious condition such as an infection or inflammation may be present. Immediately remove and examine your lenses. If a lens appears to be damaged, do not reapply; consult your eye care practitioner. If the symptom stops and the lenses appear to be undamaged, thoroughly clean, rinse and disinfect the lenses and reapply them. If the symptom continues, immediately remove your lenses and consult your eye care practitioner for professional identification of the symptom and begin treatment, if necessary, to avoid serious eye damage. For more information, see your Instructions for Wearers booklet for your specific contact lenses.

How Supplied: Sterile in 30 or 50 single-use containers of 0.01 fl oz each.

(logo) ALLERGAN

Irvine, California 92715, U.S.A.

Revised: 9/16/96

Refresh® CL Lubricating and Rewetting Drops (8197X)

Carton

TOP FLAP

(logo) ALLERGAN Product Number

Refresh® CL Lubricating and Rewetting Drops

USE ONLY IF TAB AND SIGNLE-USE CONTAINER ARE INTACT.

BOTTOM FLAP

Lot Number
Expiration Date

DUST FLAP

(Part Number) (Copycode)

Refresh® CL Lubricating and Rewetting Drops (8197X)

Single Use Container (Embossed Copy)

Refresh® CL Lubricating and Rewetting Drops (8197X)

(carboxymethylcellulose sodium)

Allergan, Inc.

Irvine, CA 92715

(Lot Number)

(Expiration Date)

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